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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/539,256

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EXAMINER

YOUNG, SHAWQUA

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

07/11/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/539,256

Applicant(s)

WIESNER ET AL.

Examiner

Shawquia Young

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 June 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 13-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 13-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

Claims 1-11 and 13-24 are currently pending in the instant application.

Applicants have amended claims 1-11, 13 and 19-24 in an amendment filed on June 19, 2007. The Examiner has withdrawn the finality of the last Office Action mailed April 19, 2007. Upon reexamining the instant claims, the Examiner has reopened prosecution and a new ground(s) of rejection is made which will be discussed in more detail below.

I. *Response to Arguments*

Applicant's arguments, filed June 19, 2007 with respect to the rejection of claims 19 and 21 under 35 USC 112, first paragraph for scope of enablement and the rejection of claims 1, 3-9, 11, 19, 20 and 23 under 35 USC 112, second paragraph as being indefinite have been fully considered and are persuasive. The rejection of claims 19 and 21 under 35 USC 112, first paragraph for scope of enablement and the rejection of claims 1, 3-9, 11, 19, 20 and 23 under 35 USC 112, second paragraph as being indefinite have been withdrawn.

The Examiner wants to confirm with Applicants that the rejection of claim 24 under 35 USC 112, first paragraph, written description is withdrawn.

As mentioned above, upon further examination of the current amendments to the claims, a new ground(s) of rejection is made in view of claims 1-11 and 13-24 under 35 USC 112, second paragraph for being indefinite, a rejection of claim 5 under 35 USC 112, second paragraph for lacking antecedent basis, a rejection of claims 13-18 under

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35 USC 112, first paragraph, enablement and a rejection of claim 23 under 35 USC 112, second paragraph for being indefinite.

II. Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,

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3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case

The nature of the invention

The nature of the invention is a method of treating or preventing a disease comprising administering an effective dose of the compound, salt, solvate or prodrug of claim 1 to a subject in need thereof, wherein the disease is selected from the group consisting of a gastrointestinal tract disease, a urinary tract disease, a digestive disorder and a disease associated with severe pain or conditions or pain.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In *re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is

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the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of any condition mediated by kappa receptor activity, whether or not the condition is effected by the activity at kappa receptors would make a difference.

Applicants are claiming a method of treating or preventing a disease wherein the disease is selected from the group consisting of a gastrointestinal tract disease, a urinary tract disease, a digestive disorder and a disease associated with severe pain or conditions of pain. For example, digestive disorders consist of various diseases such as Irritable Bowel Syndrome, Crohn's disease, dyspepsia, stomach cancer, etc.

<URL:<http://familydoctor.org/online/famdocen/home/common/digestive.html>>

Diseases associated with severe pain or conditions of pain encompasses a wide range of diseases such as cancer, systemic lupus erythematosus, etc.

Applicants' claims also include the treatment or prevention of any cancer. The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. Cancer is a disease characterized by a population of cells that grow and divide without respect to normal limits, invade and destroy adjacent tissues, and may spread to distant anatomic sites through a process called metastasis (URL:<http://en.wikipedia.org/wiki/Cancer>>). Most cancers are named for where they start. For example, lung cancer starts in the lung, and breast cancer starts in the breast. Symptoms and treatment depend on the cancer type and how

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advanced it is (([URL:http://www.nlm.nih.gov/medlineplus/print/cancer.html](http://www.nlm.nih.gov/medlineplus/print/cancer.html)>). Treatment may include surgery, radiation, chemotherapy, immunotherapy, monoclonal antibody therapy, etc. Because "cancer" refers to a class of diseases, it is unlikely that there will ever be a single "cure for cancer". Chronic pain due to cancer is almost always associated with continuing tissue damage due to the disease process or the treatment.

Applicants claims' are to the treatment or prevention of systemic lupus erythematosus. Lupus erythematosus is a chronic autoimmune disease that is potentially debilitating and sometimes fatal as the immune system attacks the body's cells and tissue, resulting in inflammation and tissue damage. It can affect any part of the body, but most often harms the heart, joints, skin, lungs, blood vessels, liver, kidneys and nervous system. The course of this disease is unpredictable, with periods of illness (called flares) alternating with remission. Lupus erythematosus is one of the several diseases known as the great imitator because its symptoms vary so widely it often mimics or is mistaken for other illnesses, and because the symptoms come and go unpredictably. Lupus has many symptoms including joint pain or swelling, muscle pain, fever, red rashes, etc. Lupus research has dramatically increased in recent years but the exact cause of the disease is unknown and there is still no consensus on whether it is a single condition or a group of related diseases. As of 2006, there is no known cure for lupus erythematosus and treatment is restricted to dealing with the symptoms.

([URL:http://en.wikipedia.org/wiki/Lupus_erythematosus](http://en.wikipedia.org/wiki/Lupus_erythematosus)>) and

([URL:http://www.nlm.nih.gov/medlineplus/lupus.html](http://www.nlm.nih.gov/medlineplus/lupus.html)>)

Applicants are also claiming the treatment or prevention of Irritable bowel syndrome. Irritable bowel syndrome (IBS) is a common problem with the intestines. It is when the intestines squeeze too hard or not hard enough and cause food to move too quickly or too slowly through the intestines. There is no cure for IBS, but medicine can help to manage or lessen your symptoms. Common symptoms include bloating and gas, mucus in the stool, constipation, abdominal pain, diarrhea, etc. Antispasmodic medicines may be prescribed to reduce cramping if your main symptom is pain. When diarrhea is a frequent problem, anti-diarrhea medicine such as loperamide may help. Therefore, treatment of irritable bowel syndrome is based upon what symptoms the patient in need has.

(URL:<http://familydoctor.org/online/famocen/home/common/digestive/disorders/112.html>

>)

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is minimal. The specification only gives a list of conditions that can be treated by the instant invention in the specification on pages 16-25. There are no working examples present for the treatment or prevention of specific diseases or conditions.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological

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activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is method of treating or preventing a disease comprising administering an effective dose of the compound, salt, solvate or prodrug of claim 1 to a subject in need thereof, wherein the disease is selected from the group consisting of a gastrointestinal tract disease, a urinary tract disease, a digestive disorder and a disease associated with severe pain or conditions or pain.

The quantity of experimentation needed and the level of the skill in the art

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases would be benefited by the effects of binding to kappa receptors and would furthermore then have to determine which of the claimed compounds in the instant invention would provide treatment of the diseases.

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a

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patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the claims.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(1) Claims 1-11 and 13-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is drawn to "N-methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxy-pyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide comprising at least one covalently bonded acid...." The term "comprising" is unclear to the Examiner. The term "comprising" can be interpreted in more than one way. Applicant may be claiming N-methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxy-pyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide in addition to at least one covalently bonded acid which is separate from N-methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxy-pyrrolidin-1-yl)ethyl]-2,2-

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diphenylacetamide. Another way to interpret the term "comprising" is that Applicant is claiming N-methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxy-pyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide with at least one covalently bonded acid which is attached to N-methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxy-pyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide.

Furthermore, the phrase "with at least one covalently bonded acid" is unclear. According to the original disclosure on pages 7-12, there are examples where only one acid is covalently bonded to the compound N-methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxy-pyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide. The types of acid which is covalently bonded to the compound varies but the places where the acid is bonded does not vary. It is unclear if Applicants are also claiming a compound where there would be more than one acid covalently bonded on one compound or are Applicants claiming the compound N-methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxy-pyrrolidin-1-yl)ethyl]-2,2-diphenylacetamide with a covalently bonded acid where the acid may vary. Applicant is suggested to delete the term "comprising" in claim 1.

(2) Claim 5 is rejected under 35 U.S.C 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant was suggested in previous Office action to delete the term "derivative" from instant claims. It is unclear if Applicant wanted to keep the term in this claim. The term "derivative" does not appear in the independent claim 1 of which claim 5 is dependent on. Therefore, there is insufficient antecedent basis for this limitation in the claim.

(3) Claim 23 is rejected under 35 U.S.C 112, second paragraph, as being indefinite

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for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In variable R^1 , Applicants state " R^1 contains one or more functional groups in addition to the groups in addition to the group L^2 , a derivative of R^1 , which is provided fully or partly with protecting groups." It is unclear what Applicants mean by this definition. The claim contains the phrases " R^1 contains one or more functional groups" and "the group L^2 , a derivative of R^1 ". According to formula III L^2 is bonded to R^1 and is not a derivative of R^1 . The term "derivative" is not defined in the claims so as to know the metes and bounds of the claims. Also, the term "functional groups" is unclear in what is meant by "functional groups" in the definition of R^1 . The term "functional groups" is not defined in the claims so as to know the metes and bounds of the claims.

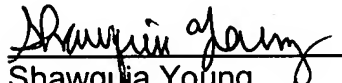
III. Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 6:00 AM-2:30PM.

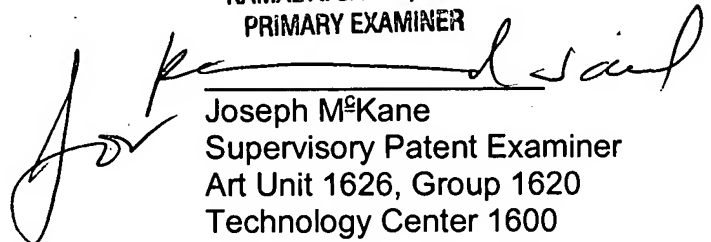
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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